

U.S.S.N. 09/858,016

Filed: May 15, 2001

AMENDMENT AND RESPONSE TO OFFICE ACTION**Remarks****Amendments to the claims**

Claims 1, 29 and 32 have been amended to clarify that the outer layer dissolves or disperses in a patient's mouth within about ten minutes after contact with the patient's saliva. Support is found at page 20, lines 1-2.

Rejections Under 35 U.S.C. § 102

Claims 1-3, 5, 7, 10, 14, 16-18 and 27 were rejected as anticipated under 35 U.S.C. §102(b) by U.S. Patent No. 5,558,879 to Chen et al. ("Chen"). Claims 1-3, 6, 8-11 and 25-29 were rejected as anticipated under 35 U.S.C. §102(b) by U.S. Patent No. 5,053,032 to Barclay et al. ("Barclay"). Claims 1-3, 5, 7, 10, 12 and 29 were rejected as anticipated under 35 U.S.C. 102(a) by EP 1112737 ("EP"). Applicants respectfully traverse the rejections if they are applied to the claims as amended.

The Claimed Invention

The claims are drawn to a pharmaceutical composition and method of manufacture. The unit dosage form has a first portion which has at least one discrete outer layer that dissolves or disperses in the mouth within 10 minutes. The first portion of the dosage form contains a therapeutically effective amount of at least one pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level. The unit dosage form has a second portion located within the first portion, which has a therapeutically effective amount of at least one pharmaceutically active ingredient capable of oral administration and which is releasable and orally ingestible by the patient after the outer layer has dispersed or has dissolved intraorally.

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Barclay

Barclay is not drawn to a device which provides for almost instantaneous release of active. As Barclay states in its objects of the invention:

"It is another object of the invention to provide an oral osmotic device having a compartment containing an active agent that can be from insoluble to very soluble in an aqueous fluid which is present in the oral cavity, and an expandable driving member consisting of a layer of a hydrophilic polymer, which operates to diminish the volume occupied by the active agent, *thereby delivering the agent from the device at a controlled rate over an extended period of time, the agent being released from the device in the form of a solution and/or suspension.* "

"The wall material may be either substantially impermeable or partially permeable to the passage of the active agent. *The wall surrounds and forms a compartment that communicates with the exterior of the device through one or more passageways in the wall.* The compartment contains an active agent exhibiting any degree of solubility in the aqueous fluid." (emphasis added)

As these passages make clear, Barclay describes an osmotic device for controlled delivery of an active beneficial agent into the oral cavity of an animal such as human (col. 4, lines 53-55). An osmotic drug delivery system uses osmotic effect of a material to force out an active agent to be delivered. As such, an osmotic drug delivery system requires an outer coating around the device that is permeable to an aqueous medium but must retain its integrity upon contact with the aqueous medium (see, for example, Carr, "Drug Delivery: A crucial role" in *Scrip Magazine*, November 1997, at <http://www.carr.pair.com/scrip.html>; and Dong, et al., "Controlled Release. L-OROS®

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SOFTCAP™ for Controlled Release of Non-Aqueous Liquid Formulations” in <http://www.drugdeliverytech.com/cgi-bin/articles.cgi?idArticle=15>). Indeed, Barclay at col. 4, lines 55-58, requires the device to have a wall formed of a material which is permeable to the passage of an external aqueous fluid which is present in the oral cavity. The wall can be removed by patient sucking in a period between 15 to 30 minutes (col. 17, lines 37-40). As such, Barclay does not have an outer layer which dissolves or disperses in the mouth within 10 minutes.

This feature is not just an “intended use”; it is a structural feature which results from the nature of the coating of the first portion, e.g., the thickness of the coating and the type of coating materials used to form the coating (see specification at p. 21, line 25 to p. 22, line 17 of the present application; see also col. 11, lines 43-46 of U.S. Patent No. 4,814,181, cited by the Examiner as prior art).

Since Barclay does not disclose an outer coating containing an active agent which dissolves to release the active agent, Barclay does not anticipate any of claims 1-3, 6, 8-11 and 25-29.

Chen

Chen describes a controlled release osmotic tablet (col. 3, lines 18-20). The tablet requires a water soluble osmotic agent (col. 3, lines 27) and is coated with *a water insoluble polymeric membrane* (col. 3, lines 32-33). The osmotic drug delivery device may provide an immediate release layer which is coated with hydroxypropyl cellulose (col. 6, lines 36-45 and 61-64; Figure 2) but this does not contain an active ingredient, as defined by the pending claims. Moreover, as shown in Figure 2 and the example (which states in relevant part: “(d) An immediate release coating is applied to the tablets

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prepared in step (c) by coating the tablets with an immediate release coating solution (IV). The coating is applied using a fluid bed coater or a perforated coating pan until the tablets exhibit a weight gain of 19.8%. Several of the coated tablets were placed in a Type II, USP dissolution apparatus having 900 ml of purified water at 37.2.degree. C. which is stirred at 100 rpm with a paddle. *After about two hours, a single aperture forms in the edge of the side of the tablet as shown in FIG. 3 and the core contents begin to extrude out of the coated tablet."* *Emphasis added*)), the immediate release portion does not dissolve or disperses within 10 minutes and release active.

In contrast, the claims define a pharmaceutical unit dosage form including an outer layer which disperses or dissolves in the patient's mouth within 10 minutes and thereby releases active ingredient.

Since Chen fails to disclose an outer layer containing active ingredient which dissolves or disperses within ten minutes upon contact with saliva, Chen fails to anticipate any of claims 1-3, 5, 7, 10, 14, 16-18 and 27.

EP 1112737

EP 1112737 ("EP") was published on July 4, 2001. An EP is available as prior art only as of its date of publication. The present application was filed on May 15, 2001, more than one month prior to the publication of EP. Therefore, the pharmaceutical composition described in EP is not prior art under 35 U.S.C. 102(a).

Rejection Under 35 U.S.C. § 103

The Examiner rejected claims 4-5, 7, 12-24, and 32 as obvious under 35 U.S.C. § 103 over Barclay in view of U.S. Pat. No. 4,814,181 to Jordan et al. ("Jordan"). The Examiner further rejected claims 4-5, 7, 12-24, and 32 as obvious over Barclay in view of

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U.S. Pat. No. 6,004,582 to Faour et al. ("Faour"). The applicants respectfully traverse the rejections if they are applied to the claims as amended.

Barclay and Chen have been discussed above.

Jordan

Jordan describes an osmotic dosage form for fast delivery of a first agent and slow delivery of a second agent (col. 2, lines 20-68; col. 3, lines 1-29; col. 4, lines 1-28).

Further, the dosage form described in Jordan is for gastrointestinal tract delivery (col. 3, lines 9-14). There is no disclosure of intraoral administration.

The Examiner asserted that Jordan is cited to show that the general concept of providing a fast release portion and a slow release portion in a drug delivery device. First, none of Barclay or Jordan provides any motivation for one of ordinary skill in the art to combine Barclay and Jordan. In fact, Barclay and Jordan are not combinable. Barclay is drawn to oral delivery of a drug. In contrast, Jordan is drawn to the delivery of a drug to the GI tract. The oral cavity and the GI tract have totally different physiological conditions: e.g., different bacterial flora, different pH, and different rate of taking up a pharmaceutically active agent. As one of ordinary skill in the art would appreciate, the need for delivery of a drug to the GI tract is based at least partially on the need to avoid or reduce systemic side effects of the drug and to reduce decomposition of the drug in areas other than the GI tract. Therefore, to combine the teachings of drug delivery devices drawn to different modes of administration would often render either Barclay or Jordan unsatisfactory for their respective intended purposes (see, In re Mills, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990); see also MPEP §2143.01).

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Second, even if there were any motivation to combine Barclay and Jordan, one of ordinary skill in the art who is in possession of Barclay and Jordan would expect that the release rate of Barclay could be manipulated through the means of Jordan, namely, a osmotic device having a fast release portion and a slow release portion. As shown in Figures 3-7 of Jordan, the fast release of the drug used therein does not occur *until at least one hour after administration*. This is consistent with the device of Jordan which is drawn to GI delivery of a drug. As such, one of ordinary skill in the art taught by Barclay and Jordan would not have a reasonable expectation of success of the subject matter defined in any of the claims, which requires the first portion of the composition to dissolve or disperse within 10 minutes following contact with saliva, to thereby release the active agent. As such, Barclay in view of Jordan would not render any of claims 4-5, 7, 12-24, and 32 *prima facie* obvious under 35 U.S.C. 103. See In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); see also MPEP §2143.

Faour

Faour describes and claims a multi-layer osmotic delivery device (col. 4, lines 63-66). The device requires a first agent containing core surrounded by a semipermeable membrane (col. 4, line 66 to col. 5, line 6). The first active agent is released through a preformed passageway in the semipermeable membrane which is generated by mechanical perforation, laser perforation or any other similar method (col. 8, lines 58-61). The outer layer does not dissolve or disperse in an aqueous environment, as required for a device which dissolves or disperses when applied to the buccal or sublingual areas of the mouth.

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In combination, Barclay and Faour would not lead to the claimed device and method of manufacture, but to an osmotic device with a water-insoluble outer layer. Accordingly, Barclay and Faour in combination do not make obvious the claimed device or method of manufacture (*see, Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986); *see also* MPEP § 2141).

The Examiner asserted that Faour was cited to show that the general concept of providing a fast release as well as a delayed release of a drug. Even if the Examiner's assertion were true, Barclay in combination of Faour would lead one of ordinary skill in the art to modify Barclay's osmotic device with the means provided in Faour to achieve a fast release and a delayed release of a drug. As discussed above, Faour describes the use a perforated water-insoluble outer layer to achieve the fast release of a drug; not an outer layer that dissolves within ten minutes of contacting saliva to provide a rapid release of an active agent within the mouth, with the second portion not being released until later. Therefore, Barclay in combination with Faour are clearly distinguishable from the subject matter defined in any of claims 4-5, 7, 12-24, and 32.

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Allowance of all claims 1-29 and 32 are earnestly solicited.

Respectfully submitted,

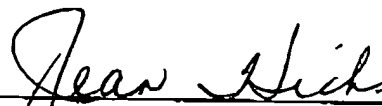


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CERTIFICATE OF FACSIMILE TRANSMISSION (37 CFR 1.8a)

I hereby certify that this Amendment and Response to Office Action, along with any paper referred to as being attached or enclosed, is being facsimile transmitted to the Commissioner for Patents on the date shown below.


Jean Hicks

Date: May 6, 2003

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